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EXAMINER	
RIGGS II, LARRY D	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/662,713	HAALAND ET AL.	
	Examiner	Art Unit	
	Larry D. Riggs II	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 July 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :17 August 2007, 21 November 2003.

DETAILED ACTION

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, (see specification, page 12, paragraph 40). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Instant claim 1 lines 7-9, claim 32 lines 6-8 recite the limitation of "mapping or maps." It unclear what "maps" means. One interpretation is that when a substance is mapped the substance is represented graphically. Another interpretation is that when a substance is mapped, the substance is has been accounted for or tracked into the statistics. For purposes of this office action, the latter interpretation is used.

Instant claim 1 line 16 recites the limitation "and/or or". It is not clear what alternative combination of limitations is claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 9-12, 15-24 and 32-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Akong et al. (US 6,127,133).

The instant claims are drawn to an automated method of identifying agents that cause a phenotypic change in a cell by using a software program for generating a computer representation of a statistical design that accounts for the type of agent used, the concentration of the agent, and the location of the agent on a receptacle array, contacting the agent with cells, obtaining data regarding the cells and their contact with the agent, then utilizing an processor with an algorithm to compare the phenotypic data and statistical design to determine the effective agents to cause phenotypic change and storing such statistical design and agent data.

Regarding claim 1, Akong et al. shows an automated method of identifying agents (defined as growth effector molecules, i.e. growth factors, extra-cellular matrix molecules, peptide, hormone and cytokines, in the specification, paragraph 25) that cause a phenotypic change in a cell, (phenotypic change is a "desired biological response", i.e. wherein molecules that bind to cell surface receptors and regulate the survival, differentiation, proliferation or maturation of these cells, as described in the specification paragraphs 32 and 35), Akong et al. shows addition of drug compounds

that affect the Muscarinic and Nicotinic receptors and calcium ion channels of various cell lines, (see Example 3, columns 23-25); by using a software program generating a computer representation of a statistical design (specification provides an example of the computer representation may be a spread sheet of the experimental design with agents, agent concentrations and wells listed, paragraphs 29 and 34) that includes generic factor names, factor levels and experimental runs on a array of wells, (see column 4, line 62 – column 5, line 31; column 7, line 49 – column 8, line 43; column 27, lines 7-12; Figures 1, 2, 5 and 7; Example 3, columns 23-25). Akong et al. shows contacting cells with drug compounds (column 9, line 28 - column 11, line 19); utilizing a microprocessor with equations, (see column 19, lines Equations 1 and 2), to compare the fluorescence data and statistical design to determine the effective drugs that affect muscarinic acetylcholine receptors, nicotinic acetylcholine receptors and calcium channels, and storing such statistical design and drug data in tables and on disk, (see column 17, lines 30-34; column 18, line 48 – column 19, line 30; columns 23-28, Tables of Examples 3 and 4; Figure 6).

Regarding claims 2 and 3, Akong et al. shows user input of the statistical design including identity and concentration of drugs into the software program, (see column 7, lines 49-62; Figure 6 and 7).

Regarding claims 4, 34 and 35, Akong et al. shows a computer program for controlling the automatic pipettor for dispensing reagents into wells based on parameters input into the software, (see column 6, lines 42-67, column 7, line 49 – column 8, line 43, column 28, lines 16; Figures 3-5).

Regarding claim 5, Akong et al. shows dispensing drug compounds into wells, (see column 6, lines 42-67; Figure 5).

Regarding claims 9 and 33, Akong et al. stores data in an integrated database, (see column 9, lines 35-45; Figure 6).

Regarding claims 10-12 and 36, Akong et al. shows the use of algorithms to statistically analyze results and compare effectiveness of drugs to change in receptor or channel binding through increased or decreased fluorescence which can be stored, (see column 17, line 30 – column 18, line 19, column 18, line 58 – column 19, line 30, equations 1 and 2).

Regarding claims 15 and 15, Akong et al. shows identification of cellular ligand, nerve growth factor, heparin binding growth factor and other grow factors which affect functional growth factor receptors, (see column 14, lines 7-12).

Regarding claims 17 and 18, Akong et al. shows variation of concentration of drugs in the experiment and repeating experiments of a single drug, (see column 27, lines 1-41, column 25, lines 40-42).

Regarding claims 19-21, Akong et al. shows automated drug screening assay for the identification of cell surface receptors, ion channels, and growth factor receptors (see column 13, lines 4-61; column 14 , lines 7-12), responsible for responsible for cellular pathway communication, from automated observation of fluorescent change associated with ion concentration change due to interaction with drug compounds, (see column 2, lines 13-30, column 12, lines 19-47, column 14, lines 13-51; Example 3, columns 23-27).

Regarding claims 22-24, Akong et al. shows identifying data on cellular mechanism proteins such as G-protein-coupled receptors (muscarinic acetylcholine receptors) and ion channel proteins, by assays comparing cells known to have or not have these receptors or channels present and be modulated by the presence of drugs, (column 11, line 51 – column 12, line 47, Example 3, columns 23-27).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akong et al. (US 6,127,133) in view of Eggers et al. (US 5,532,128).

The instant claims are drawn to an automated method of identifying agents that cause a phenotypic change in a cell by using a software program for generating a computer representation of a statistical design that accounts for the type of agent used, the concentration of the agent, and the location of the agent on a receptacle array, contacting the agent with cells, obtaining data regarding the cells and their contact with the agent, then utilizing an processor with an algorithm to compare the phenotypic data and statistical design to determine the effective agents to cause phenotypic change and storing such statistical design and agent data.

Regarding claim 1, Akong et al. shows an automated method of identifying agents (defined as growth effector molecules, i.e. growth factors, extra-cellular matrix molecules, peptide, hormone and cytokines, in the specification, paragraph 25) that cause a phenotypic change in a cell, (phenotypic change is a "desired biological response", i.e. wherein molecules that bind to cell surface receptors and regulate the survival, differentiation, proliferation or maturation of these cells, as described in the specification paragraphs 32 and 35), Akong et al. shows addition of drug compounds that affect the Muscarinic and Nicotinic receptors and calcium ion channels of various cell lines, (see Example 3, columns 23-25); by using a software program generating a

computer representation of a statistical design (specification provides an example of the computer representation may be a spread sheet of the experimental design with agents, agent concentrations and wells listed, paragraphs 29 and 34) that includes generic factor names, factor levels and experimental runs on a array of wells, (see column 4, line 62 – column 5, line 31; column 7, line 49 – column 8, line 43; column 27, lines 7-12; Figures 1, 2, 5 and 7; Example 3, columns 23-25). Akong et al. shows contacting cells with drug compounds (column 9, line 28 - column 11, line 19); utilizing a microprocessor with equations, (see column 19, lines Equations 1 and 2), to compare the fluorescence data and statistical design to determine the effective drugs that affect muscarinic acetylcholine receptors, nicotinic acetylcholine receptors and calcium channels, and storing such statistical design and drug data in tables and on disk, (see column 17, lines 30-34; column 18, line 48 – column 19, line 30; columns 23-28, Tables of Examples 3 and 4; Figure 6).

Akong et al. does not show drugs covalently immobilized onto biocompatible polymer coated wells.

Eggers et al. provides a multi-site detection method and apparatus for identifying molecular structures. Eggers et al. shows culture surface wells coated with a biocompatible agent-immobilized material, (see column 7, line 60-couumn 8, line 67; Figures 6 and 7). Eggers et al. shows biocompatible agent-immobilized material containing reactive groups for covalently immobilizing agents, (see column 7, line 60-couumn 8, line 67; Figures 6 & 7).

Claims 1, 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akong et al. in view of Eggers et al. as applied to claims 1 and 6-8 above, and further in view of Ali et al. (US 6,448,983).

The claims are drawn to a method of various statistical designs for identifying agents that cause a phenotypic change in a cell.

Akong et al. in view of Eggers et al. as applied to claims 1 and 6-8 above does not show various statistical designs for identifying agents that cause a phenotypic change in a cell.

Ali et al. shows a method for selection of an experimental design on a statistical based approach. Ali et al. shows statistical designs of Plackett-Burman and space-filling design of face centered designs, (see column 1, lines 5-41, column 4, lines 39-59; Figures 1 and 2).

Claims 1 and 25-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akong et al. in view of Eggers et al. as applied to claims 1 and 6-8 above, and further in view of Fink et al. (US 5,808,918).

The claims are drawn to a method for identifying agents that cause a phenotypic change in a cell, wherein a program calculates, from stored scientific information, (scientific information may come from experimental data or scientific literature, see specification, paragraph 36), the likelihood that a cellular pathway, protein, gene or receptor is involved with the phenotypic cellular changes.

Akong et al. in view of Eggers et al. as applied to claims 1 and 6-8 above does not show a program for calculating, using stored scientific information, the likelihood that

a cellular pathway, protein, gene or receptors, is involved in phenotypic changes of a cell associated with an agent, (specification provides that this determination can be a computer executable model as described in US 5,808,918, incorporated by reference, paragraph 36).

Fink et al. provides a hierarchical biological modeling system and method from information and structures based on multiple sources. Fink et al. shows that from an interactive model originating from scientific data, including experiments and scientific literature, that biological targets for drug development can be identified and subcellular phenomena can be observed, (see column 12, line 44 – column 13, line 60; Figures 5-7).

Claims 1, 30 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akong et al. in view of Eggers et al. as applied to claims 1 and 6-8 above, and further in view Terramani, et al. *In Vitro Cell. Dev. Biol.; Human Macrovascular Endothelial Cells: Optimization of Culture Conditions*, 2000, 36, 125-132.

The claims are drawn to a method for identifying agents that cause a phenotypic change in a cell, wherein the phenotypic data, acquired by immunocytochemistry analysis, determines biological markers indicating proliferation and/or differentiation of the cells.

Akong et al. in view of Eggers et al. as applied to claims 1 and 6-8 above does not show data acquired by immunochemistry analysis indicating biological markers indicative of proliferation of differentiation of cells in the presence of agents.

Terramani, et al. provides a study to identify optimal culture conditions to support the proliferation of human macrovascular endothelial cells. Terramani, et al. shows data acquired by immunochemistry analysis indicating biological marker, vWF when staining HSVEC and HUVEC cells in their use of proliferation studies with cellular mitogens, (see page 126, left column, last full paragraph – right column, third paragraph).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the process and system of drug identification of Akong et al. by coating wells with drugs covalently bound to polymers as shown by Eggers et al. because Eggers et al. shows that covalently binding molecules to a surface enables greater efficiency and sensitivity to identification of molecular structures. It would have been further obvious to modifying the process of Akong et al. in view of Eggers et al. as applied to claims 1 and 6-8 above, through various statistical designs as shown by Ali et al. to increase the efficiency of drug identification. It would have been further obvious to modifying the process of Akong et al. in view of Eggers et al. as applied to claims 1 and 6-8 above, by incorporating a software program to identify possible biological targets, as shown by Fink et al. to provide a better reasoning of the impact of the drug on a cellular system. It would have been further obvious to modifying the process of Akong et al. in view of Eggers et al. as applied to claims 1 and 6-8 above, by using immunochemistry analysis as shown by Terramani, et al. to better understand the cellular impact of the drug.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry D. Riggs II whose telephone number is 571-270-3062. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LDR/
Larry D. Riggs II
Examiner, Art Unit 1631

/John S. Brusca/
Primary Examiner
Art Unit 1631